UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

IN THE MATTER OF:	)	
	)	Docket No. TSCA-HQ-2010-5022
	)	
Elementis Chromium Inc.	)	
f/k/a Elementis Chromium, L.P.,	)	
	)	
	)	
Respondent.	)	
	)	

RESPONDENT'S MEMORANDUM IN OPPOSITION TO COMPLAINANT'S MOTION FOR ACCELERATED DECISION ON LIABILITY

Respondent, Elementis Chromium Inc.[1] ("Respondent" or Elementis"), respectfully submits this memorandum in opposition to the Motion for Accelerated Decision on Liability (the "Motion") filed by the United States Environmental Protection Agency ("Complainant" or "EPA"), and requests that an order be issued denying the Motion.

I. INTRODUCTION

This enforcement action has been brought by the United States Environmental Protection Agency ("Complainant" or "EPA") against Elementis for alleged violation of Section 15(c) of the Toxic Substances Control Act ("TSCA"), 15 U.S.C. § 2614(c). EPA alleges that Elementis was required by Section 8(e) of TSCA to submit the *"Collaborative-Cohort Mortality Study of Four Chromate Production Facilities, 1958-1998, Final Report"* prepared by Applied Epidemiology dated September 27, 2002 (the

[1] Elementis Chromium LP was merged into Elementis Chromium GP Inc. on September 10, 2010. Elementis Chromium GP Inc. then changed its name to Elementis Chromium Inc.

"Report") to EPA. EPA further claims that the Report contains information which reasonably supports the conclusion that hexavalent chromium presents a substantial risk of injury to health or the environment. Complainant has filed a Motion for Accelerated Decision on the grounds that there are no genuine issues of material fact and it is entitled to judgment in its favor as a matter of law.

II. SUMMARY OF ARGUMENT

Elementis does not contest that it is a manufacturer of chromium chemical products, including some that contain hexavalent chromium, or that it received the Report on October 8, 2002. Further, Elementis concedes that it did not submit the Report to EPA until November 17, 2008 in response to a subpoena from EPA to one of Elementis' employees.

However, genuine issues regarding material facts exist and therefore preclude granting EPA's Motion. Specifically, the evidence in this matter will establish that Elementis was not required to submit the Report to EPA under Section 8(e) of TSCA because the only information contained in the Report supporting the conclusion that hexavalent chromium presents a substantial risk of injury to health was already very well known to EPA, and Elementis had actual knowledge of EPA's awareness of the information. The only information in the Report reasonably supporting the conclusion that hexavalent chromium presents a substantial risk of injury to human health was the finding by Applied Epidemiology that there was a statistically significant increased incidence of lung cancer in the employees exposed to high levels of hexavalent chromium in the chromium plants in Germany. This increased incidence of lung cancer in persons exposed to high levels of chromium had been found in *many* prior epidemiologic studies known to EPA (including one that was actually *funded* by EPA), and Elementis had actual knowledge that such studies were in EPA's possession.

In fact, one such study, completed just two years prior to the Report and paid for with EPA funds, was prepared in part by an employee of EPA, Dr. Herman Gibb (the "Gibb Study"). When Dr. Joel Barnhart, Vice President-Technical for Elementis, received the draft Report from Applied Epidemiology in April 2002, he analyzed the Report, and determined that its reasonably supportable conclusions were no different than those identified by epidemiologic studies with which he was already familiar, especially the Gibb Study. As Dr. Barnhart knew that EPA already had the Gibb Study in its possession, he determined that there was no obligation to provide the Report to EPA pursuant to Section 8(e) of TSCA.

Dr. Barnhart also had serious concerns about the combined data sets used in the Report, as did its principal author, Dr. Kenneth Mundt, and thus believed that the study, as a whole, was flawed. Given the fact that EPA was already well aware of the belief that exposure of persons to high levels of hexavalent chromium could lead to an increased risk of developing lung cancer, Dr. Barnhart and Elementis chose not to submit the Report to EPA pursuant to TSCA Section 8(e).

The facts are clear that: 1) EPA was fully aware of the belief that exposure to high levels of hexavalent chromium increases the risk of contracting lung cancer at the time Elementis received the Report, 2) Elementis had actual knowledge that this information was known to EPA, and 3) this was the only information in the Report which reasonably supports the conclusion that hexavalent chromium presents a substantial risk of injury to health. Therefore, the only possible conclusion is that Elementis had no obligation to provide the Report to EPA. EPA misconstrues the information contained in the Report, and incorrectly concludes that such information is "substantial risk" information not previously known by EPA. As such, genuine issues as to some material facts exist, and Complainant's Motion for Accelerated Decision on Liability should be denied.

III. STATEMENT OF FACTS

Elementis is a manufacturer, processor and distributor of chromium chemical products, including chromic oxide, chromic acid and sodium dichromate. Barnhart Aff., Ex. A, ¶ 3. Elementis and its predecessors have been manufacturing chromium chemical products for more than 35 years. Barnhart Aff., Ex. A, ¶ 4.

Elementis was a member of the Industrial Health Foundation ("IHF") Chromium Chemicals Health and Environmental Committee from at least 1984 until 2003 when IHF was dissolved in bankruptcy. Barnhart Aff., Ex. A, ¶ 5. Other chromium chemical manufacturers that were members of the IHF Chromium Chemicals Health and Environmental Committee were Bayer AG and Occidental Chemical Corporation.[2] Barnhart Aff., Ex. A, ¶ 6.

In 1998, the IHF Chromium Chemicals Health and Environmental Committee initiated an epidemiology study involving two chromium chemicals manufacturing plants located in the United States (Castle Hayne, North Carolina and Corpus Christi, Texas), two chromium chemicals manufacturing plants located in Germany (Leverkusen and Uerdingen) and one chromium chemicals manufacturing plant in the United Kingdom

[2] Complainant has not brought an enforcement action against either Bayer AG or Occidental, even though both of those companies were chromium chemical manufacturers, processors and distributors, they both received the Report at exactly the same time as Elementis, and did not provide the Report to EPA.

(Eaglescliffe, England). Barnhart Aff., Ex. A, ¶ 7. The IHF Chromium Chemicals Health and Environmental Committee's purpose in commissioning the epidemiology study was to conduct a large study to better assess and understand the cancer risk associated with exposure to hexavalent chromium at the facilities involved in the study.[3] Barnhart Aff., Ex. A, ¶ 8; Mundt Aff., Ex. B, ¶ 5. Applied Epidemiology Inc. (which later became part of ENVIRON International Corporation) entered into an agreement with IHF to undertake this work. Barnhart Aff., Ex. A, ¶ 8; Mundt Aff., Ex. B, ¶ 5.

Applied Epidemiology was retained by the IHF to analyze reported cases of lung cancer in workers at the plants and exposure levels of those workers to hexavalent chromium compounds to determine whether any statistically significant correlation could be found.[4] Report, p. 2 (attached to Complainant's Memorandum in Support of the Motion at Ex. 1). One significant challenge of the study was that worker exposure in the United States plants had been measured by personal air monitors, while the primary measure of exposure in the German plants was through analysis of chromium in the urine of the workers. Mundt Aff., Ex. B, ¶ 7. In order for Applied Epidemiology to analyze the entire data set as one, it had to create a conversion factor to convert air concentrations measured by the personal air monitors to urine cadmium levels. Mundt Aff., Ex. B, ¶ 8. This required Applied Epidemiology to make some very substantial assumptions. Id. After making such assumptions, it came up with a single conversion factor that it used to

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[3] On July 24, 1998, the chair of IHF Chromium Chemicals Health and Environmental Committee, Bruce Norman, wrote to EPA, the federal Occupational Safety and Health Administration ("OSHA") and other regulatory bodies informing them of the initiation of the study. Barnhart Aff., Ex. A, ¶ 9.

[4] In 1999, it became apparent that the data from the Eaglescliffe, England plant would not be compiled in time to be included in the study, so it was eliminated from the study. Barnhart Aff., Ex. A; ¶ 10, Mundt Aff., Ex. B, ¶ 6.

convert all of the air monitoring exposure valuations to urine chromium levels. Mundt Aff., Ex. B, ¶ 9.

Applied Epidemiology then broke the cohort into four different groups based on relative exposure levels: low (0 - 39.9 μg/L), intermediate-low (40.0 - 99.9 μg/L), intermediate – high (100.0 – 199.9 μg/L) and high (≤ 200.0 μg/L). Mundt Aff., Ex. B, ¶ 10; Report p. 99 (attached to Complainant's Memorandum in Support of the Motion at Ex. 1). For each exposure group, Applied Epidemiology then compared the number of persons within each group who had contracted lung cancer with the number of people that would be expected to contract lung cancer in the group based on statistics from the general population in the locals where the plants were situated. Mundt Aff., Ex. B, ¶ 10.

The highest exposure group, the persons with exposures of ≥200 μg/L, contained a total of 117 workers. Mundt Aff., Ex. B, ¶ 11. Of this number of workers, there were 12 reported cases of lung cancer. Id. When compared with the number of cases that would be expected in the general population based on historical reporting, 5.72 expected cases, Applied Epidemiology concluded that number of actual cases of lung cancer in this group indicated that there was an elevated risk of contracting lung cancer exhibited by this group. Mundt Aff., Ex. B, ¶ 11.

Importantly, none of the other groups showed a statistically significant increase in the number of cancer cases. Mundt Aff., Ex. B, ¶ 12. Specifically, the exposure group 0-39.9 μg/L had 4 reported cases of lung cancer, with 6.97 expected, the exposure group 40-99.9 μg/L, had 4 reported cases of lung cancer, with 4.20 expected, and the exposure group 100-199.9 μg/L, had 5 reported cases, with 5.30 expected. Id.

In early 2002, Applied Epidemiology provided a draft of the Report to the IHF Chromium Chemicals Health and Environmental Committee.[5] Barnhart Aff., Ex. A, ¶ 11; Mundt Aff., Ex. B, ¶ 14. The final Report was e-mailed to the members of the IHF Chromium Chemicals Health and Environmental Committee on October 8, 2002 and then presented, in person, by Dr. Kenneth Mundt of Applied Epidemiology at the IHF Chromium Chemicals Health and Environmental Committee meeting on October 15, 2002. Mundt Aff., Ex. B, ¶ 15. During the October 15, 2002 meeting, Dr. Mundt reported to the IHF Chromium Chemicals Health and Environmental Committee that he had presented the results of the study at the EPICOH international conference on Epidemiology in Barcelona, Spain in the previous month. Barnhart Aff., Ex. A, ¶ 12; Mundt Aff., Ex. B, ¶ 17. This conference is a periodic gathering of the world's preeminent occupational epidemiologists. Id. *See also* www. epicoh.org. He further reported that epidemiologists at the meeting questioned the propriety of combining the German plant cohort with the cohort from the United States plants because of the different methods used to measure exposure in the two cohorts. Mundt Aff., Ex. B, ¶ 19.

Before the October 15, 2002 meeting of the IHF Chromium Chemicals Health and Environmental Committee, and at the meeting, the IHF Chromium Chemicals Health and Environmental Committee discussed with Dr. Mundt the proposition that the study be divided into parts for publication since the German exposure levels were significantly higher and the data was primarily urinary chromium measurements, while the US exposure levels were lower and based on air sampling data. Barnhart Aff., Ex. A, ¶ 13;

[5] Applied Epidemiology also provided draft copies to the scientific advisory board ("SAB") convened by Applied Epidemiology. The SAB was made up of James Stewart, Ph.D. of Harvard University, Harvey Checkoway, Ph.D. of the University of Washington and Edwin van Wijingaarden, Ph.D. of the University of North Carolina for review and comment. Barnhart Aff., Ex. A; ¶ 11, Mundt Aff., Ex. B, ¶ 14.

Mundt Aff., Ex. B, ¶ 18. The IHF Chromium Chemicals Health and Environmental Committee also discussed the complications and problems associated with correlating urinary chromium measurements with air sampling data. Barnhart Aff., Ex. A, ¶ 13; Mundt Aff., Ex. B, ¶ 19. Dr. Mundt confirmed that similar concerns and issues had been discussed with him by peers at the September 2002 EPICOH conference. Mundt Aff., Ex. B, ¶ 19.

When Dr. Barnhart received the draft Report in early 2002, he compared the results to the results reported by the Gibb Study. Barnhart Aff., Ex. A, ¶ 15. The only information from both of these studies that reasonably supports a conclusion that hexavalent chromium presents a "substantial risk of injury to health" is that persons subject to higher exposure levels have an increased incidence of lung cancer. Barnhart Aff., Ex. A, ¶ 16. This could lead to the conclusion that high levels of exposure to hexavalent chromium causes increased risk of lung cancer. Barnhart Aff., Ex. A, ¶ 17; Report p. 84 (attached to Complainant's Memorandum in Support of the Motion at Ex. 1). As the Gibb Study had already identified this potential risk, and Dr. Barnhart knew EPA had the Gibb Study because he knew Dr. Gibb worked for EPA and EPA had funded the Gibb Study, Dr. Barnhart concluded that the Report did not need to be provided to EPA pursuant to TSCA section 8(e). Barnhart Aff., Ex. A; ¶ 18, Gibb Aff., Ex. C, ¶ 9.

In 2003, IHF went bankrupt and disbanded, and Applied Epidemiology was acquired by ENVIRON International Corporation. Barnhart Aff., Ex. A, ¶ 19; Mundt Aff., Ex. B, ¶ 3. The IHF Chromium Chemicals Health and Environmental Committee did not meet again after the October 15, 2002 meeting. Barnhart Aff., Ex. A, ¶ 20.

IV. ARGUMENT

A. Standard Of Review

The Presiding Officer may grant a motion for accelerated decision if "no genuine issue of material fact exists and a party is entitled to judgment as a matter of law." 40 C.F.R. § 22.20(a).

Motions for accelerated decision under 40 C.F.R. § 22.20(a) are treated similar to motions for summary judgment under Rule 56 of the Federal Rules of Civil Procedure ("FRCP"). *See, e.g.,* In re BWX Tech., Inc., 9 E.A.D. 61, 74-75 (EAB 2000); Belmont Plating Works, Docket No. RCRA-5-2001-0013, 2002 EPA ALJ LEXIS 65, at *8 (EPA ALJ Sept. 11, 2002); Pursuant to FRCP 56(a), "[t]he court shall grant summary judgment if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." For that reason, federal court decisions interpreting Rule 56 provide guidance for adjudicating motions for accelerated decision. *See* CWM Chem. Serv., 6 E.A.D. 1 (EAB 1995).

The burden of showing that no genuine issue of material fact exists is on the party moving for summary judgment. Adickes v. S. H. Kress & Co., 398 U.S. 144, 157 (1970). In determining whether the movant has met its burden, the Court views the evidence in the light most favorable to the nonmoving party. *See* Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1985); Adickes, 398 U.S. at 158-59. When conflicting inferences may be drawn from the evidence, summary judgment is not appropriate. Rogers Corp. v. EPA, 275 F.3d 1096, 1103 (D.C. Cir. 2002). In support of, or in opposition to, a motion for summary judgment, a party must provide evidence in support of its assertion "that a fact cannot be or is genuinely disputed by: (A) citing particular parts of materials in the record . . . or (B) showing that the materials cited do not establish the absence or presence of a genuine dispute, or that an adverse party cannot produce admissible evidence to support the fact." FRCP 56(c)(1)(A) and (B).

B. Genuine Issues Of Material Fact Exist Because Elementis Was Not Required To Provide The Report To EPA Under Section 8(e) Of TSCA As Elementis Knew That The Substantial Risk Information In The Report Was Already Well Known To EPA.

Section 8(e) of TSCA is a one-sentence provision that reads as follows:

> Any person who manufactures, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the Administrator of such information *unless such person has actual knowledge that the Administrator has been adequately informed of such information.*

15 U.S.C. § 2607(c) (emphasis added). Thus, in order to establish a violation of this provision, the following elements must be proven:

- Alleged violator is a person who manufactures, processes or distributes in commerce a chemical substance or mixture;
- Alleged violator obtains information that reasonably supports the conclusion that a chemical substance or mixture that it manufactures, processes or distributes in commerce presents a substantial risk of injury to health; and
- Alleged violator fails to immediately notify the Administrator of the information.

However, the statute also provides that a manufacturer, processor or distributor does not have to provide substantial risk information if such information was known to the Administrator and the alleged violator had actual knowledge that such information was known to the Administrator. Thus, it is an absolute defense to an allegation of violation of TSCA Section 8(e) if the alleged violator can show that the substantial risk information was already known to EPA and the alleged violator knew this.

In this case, there is no dispute that Elementis is a manufacturer, processor and distributor in commerce of hexavalent chromium-containing chemicals. Nor is there any dispute that Elementis received the Report in October 2002 and did not provide it to the Administrator until November 18, 2008, when it responded to a subpoena from EPA. There is, however, clear factual dispute between the EPA and Elementis on three critical factual issues: 1) what information the Report contained that reasonably supports the conclusion that hexavalent chromium presents a substantial risk to health (the "Substantial Risk Information"); 2) whether the Substantial Information Risk information was already known to EPA; and 3) whether Elementis had actual knowledge that the Substantial Risk Information was already known to EPA.

1. The Only Substantial Risk Information in the Report is That Persons Exposed to High Cumulative Levels of Hexavalent Chromium Have an Increased Risk of Lung Cancer.

The epidemiologic study conducted by Applied Epidemiology analyzed workers at four chromium chemicals manufacturing plants. Mundt Aff., Ex. B, ¶¶ 4 and 6. The study quantified cumulative exposures of those workers to hexavalent chromium and then identified any of the workers who have contracted lung cancer. *See generally* the Report (attached to Complainant's Memorandum in Support of the Motion at Ex. 1). By comparing the number of actual lung cancer cases found with an expected number of lung cancer cases determined from data about lung cancer in the general population in the vicinity of the plants, Applied Epidemiology drew conclusions about the relative effect of exposure to hexavalent chromium on a worker's risk of developing lung cancer. Mundt Aff., Ex. B ¶¶ 11 and 12.

The Report, which detailed the results of the study and analysis conducted by Applied Epidemiology concluded that workers in the cohort who had been subjected to high levels of cumulative exposure to hexavalent chromium showed an increased incidence of lung cancer when compared to the general population where the plants were located. Barnhart Aff., Ex. A, ¶ 16; Mundt Aff., Ex. B, ¶ 11. Persons in the three other exposure groups did not show a statistically significant increased incidence of cancer when compared to the general population. Mundt Aff., Ex. B, ¶ 12. The Report concludes that exposure to high levels of hexavalent chromium leads to an increased risk of lung cancer. Barnhart Aff., Ex. A, ¶ 16. This conclusion identifying an elevated risk of lung cancer in the highest cumulative exposure group is the only Substantial Risk Information in the Report. Id.

EPA contends that the Report's "finding of increased lung cancer mortality risk constitutes new information about potential health risks associated with occupational exposure to hexavalent chromium under modern plant conditions" is inapposite to this case. Complainant's Memorandum in Support of the Motion, p. 25. Section 8(e) of TSCA addresses substantial risk information associated with a "chemical substance or mixture" not with processes or exposures involving a chemical substance or mixture. If a chemical is believed to cause lung cancer when inhaled, it does not matter to that finding how the inhalation occurs — the chemical still causes lung cancer. Moreover, modern plant conditions had been analyzed by EPA in connection with the Gibb Study. Gibb Aff., Ex. C, ¶ 12.

2. The Substantial Risk Information Contained in The Report Was Well Known to EPA.

Hexavalent chromium has been known to be a cause of lung cancer, and this has been known to EPA for many years. Gibb Aff., Ex. C, ¶ 10. In addition, to EPA, it is irrelevant how "modern" a facility is — EPA takes the position that any exposure to hexavalent chromium presents some risk of lung cancer. Gibb Aff., Ex. C, ¶ 10. For EPA to now take the position that the Report contains new information on substantial risk of injury from hexavalent chromium is disingenuous. As Dr. Gibb, an epidemiologist for EPA for 30 years, states, the Report "does not add to the knowledge base on the lung cancer risk from occupational exposure to hexavalent chromium." Gibb Aff., Ex. C, ¶ 9.

A very comprehensive and substantial epidemiologic study was conducted by Dr. Gibb when he worked for the National Center for Environmental Assessment at EPA on a chromium chemicals producing plant located in Baltimore, Maryland (the "Gibb Study"). Gibb Aff., Ex. C, ¶ 8, Ex. D. EPA funded this study pursuant to grant number C8822033-01, and the study was completed in 2000. Gibb Aff., Ex. C, ¶ 8, Ex. D, p. 115, FN #3. The Gibb Study "confirms the elevated lung cancer risk from hexavalent chromium exposure observed in other studies and presents the best opportunity to date of evaluating the lung cancer exposure-response relationship from exposure to hexavalent chromium." Ex. D, p. 124. Furthermore, when the exposure groups in the Gibb Study are compared with those in the Report, it is clear that the Substantial Risk Information in the Report was also found in the Gibb Study. Barnhart Aff., Ex. A, ¶ 15.

3. Elementis Knew That The Substantial Risk Information Was Already Known By EPA.

At the time of his receipt of the Report in October 2002, Dr. Barnhart compared the Substantial Risk Information in the Report with the findings of the Gibb Study and concluded that the Substantial Risk Information was already contained in the Gibb Study. Barnhart Aff., Ex. A, ¶ 15. Furthermore, Dr. Barnhart knew that EPA had the Gibb Study in its possession at the time because: a) the Gibb Study was completed in 2000, two years before Dr. Barnhart received the Report; b) at the time the Gibb Study was prepared, Dr. Gibb was employed by EPA; and 3) EPA funded the Gibb Study. Gibb Aff., Ex. C, ¶ 8.

Therefore, based on the plain language TSCA 8(e), and, more importantly, its mandate that Substantial Risk Information does not need to be provided to EPA if such Substantial Risk Information is already known to EPA, Dr. Barnhart correctly concluded that Elementis had no obligation to provide the Report to EPA.

C. EPA's Own Guidance Supports Elementis' Decision That TSCA Section 8(e) Did Not Require It To Provide The Report To EPA.

EPA has never issued any regulations elaborating on Section 8(e) of TSCA. It has, however, issued a "guidance" document, first on March 16, 1978, entitled "Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk," 43 FR 11110-11116 (March 16, 1978), and an amendment thereto on June 3, 2003, entitled "TSCA Section 8(e); Notification of Substantial Risk; Policy Clarification and Reporting Guidance," 68 FR 33129-33314 (June 3, 2003). One of the stated purposes of the revision was to "address ... which certain information need not be reported to EPA under section 8(e) of TSCA." 68 FR 33129, 33129 (June 3, 2003). Further, in the 2003 revision, EPA stated that "[s]ince the policy statement was published in 1978, this republication is intended to ensure that a single reference source for the TSCA section 8(e) policy and guidance is easily available to the regulated community and other interested parties."[6]

[6] In its Memorandum in Support of Motion for Accelerated Decision, EPA extensively cites to its guidance as support for its position that the Report should have been provided to EPA by Elementis. Complainant's Memorandum in Support of the Motion, pp. 15-16. However, it then provides that, to the extent that Elementis attempts to rely on the guidance, "guidance does not impose any binding requirements upon either the regulated community or the Agency." Complainant's Memorandum in Support, p. 29. In light of the fact that EPA has not promulgated any regulations on the one-sentence provision of Section 8(e), it is disingenuous, at best, for EPA to take the position that the regulated community cannot rely on EPA's guidance.

In the 2003 guidance document, EPA states that:

> "Substantial risk" information need not be reported under section 8(e) if it:
>
> * * *
>
> (b) Corroborates (i.e., substantially duplicates or confirm) in terms of, for example, route of exposure, dose, species, strain, sex, time to onset of effect, nature and severity of effect, a well-recognized/well-established serious adverse effect for the chemical(s) under consideration . . . .

68 FR 33,129, 33,139 (June 3, 2003). As explained by Dr. Barnhart, and confirmed by Dr. Gibb, the substantial risk information contained in the Report, namely that higher levels of exposure to hexavalent chromium is linked to increased incidence of lung cancer, was a risk that had been identified by many epidemiology studies before, was well-recognized and well-established, and was clearly known by the EPA. Barnhart Aff., Ex. A, ¶¶ 16 -18; Gibb Aff., Ex. C, ¶ 10.[7]

Issues associated with potential occupational exposure to hexavalent chromium have been appreciated for many years. OSHA set the first Permissible Exposure Limit ("PEL") for hexavalent chromium in 1971, almost 40 years ago. 36 FR 10466 (May 29, 1971). Many, many studies have been done concerning the adverse health effects of

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[7] In the "Frequently Asked Questions" ("FAQ") of its website on TSCA 8(e), EPA has clearly indicated that health assessment information, such as epidemiologic studies, are generally not reportable under TSCA § 8(e). In response to the FAQ, "[w]ould industrial hygiene assessments need to be considered for TSCA § 8(e)," EPA responded as follows:

> Typically no. Such assessments are often conducted in situations where potential exposure to the chemical has already been identified. For example, contamination of workplace air or surfaces by substances known to the manufacturer and EPA, such as Occupational Safety and Health Administration (OSHA) regulated substances, would not need to be examined for §8(e) reporting under Part V. (b)(1) of the TSCA Section 8(e) Reporting Guidance because they are not "previously unsuspected." However, information should be considered for reporting if it reasonably supports a conclusion of substantial risk (combination of toxicity and exposure) that was previously unknown. In order for workplace situation to be reportable under TSCA §8(e), it would need to be previously unsuspected and involve serious toxic effects. Also, a sudden release of a large quantity of an OSHA regulated substance may need to be considered for TSCA §8(e) reporting as an emergency incident of contamination, depending on the quantity and toxic properties of the substance.

http://www.epa.gov/opptintr/tsca8e/pubs/frequentlyaskedquestionsfaqs.html.

chromium going back more than 60 years. Ex. D, p 116; Gibb Aff., Ex. C, ¶ 10. The adverse health effects include the potential for increased risk of lung cancer for high exposure first discussed by the Public Health Service 60 years ago, and confirmed by the Gibb Study in 2000. Ex. D, p. 116; Gibb Aff., Ex. C, ¶ 10. The Report simply re-identifies this substantial risk, and thus, even by EPA's own guidance, is not something to be reported under TSCA section 8(e).

D. Information About Exposure Does Not Constitute Substantial Risk Information.

EPA spends much of its brief arguing that this phenomenon had never been identified in the "low-lime" process. However, TSCA Section 8(e) requires disclosure of information about "chemical substance or mixture," not the processes generating exposure. Every single chromium chemical manufacturing process is different in some way, and every individual's exposure is unique. TSCA Section 8(e), however, is chemical-specific, not process-specific. Thus, the fact that Applied Epidemiology looked at plants that were different than those looked at by the Gibb Study or the other chromium epidemiologic studies is irrelevant, because the health effect observed by both was the same: respiratory exposure to hexavalent chromium at certain levels leads to an increased risk of lung cancer. Under a plain reading of the statute, and EPA's own guidance, it is indisputable that Elementis had no obligation to provide the Report to EPA.

V. CONCLUSION

Elementis, a chromium chemicals manufacturer, received the Report in October 2002, and the Report contained a finding that, based on its analysis of workers at four chromium chemicals manufacturing plants, high cumulative levels of respiratory exposure to hexavalent chromium correlates with an increased risk of lung cancer. Although this finding may constitute information on substantial risk under Section 8(e) of TSCA, Elementis was under no obligation to provide the Report to EPA because this information on the substantial risk associated with hexavalent chromium was already very well known to EPA and well established within the scientific community, and Elementis had actual knowledge that EPA was in possession of such information. Given that there is a genuine issue on the material facts establishing Elementis' defense to EPA's allegation that Elementis violated Section 8(e) of TSCA, EPA's Motion for Accelerated Decision on Liability must be denied.

WHEREFORE, Elementis respectfully requests that the Presiding Officer issue an order denying Complainant's Motion for Accelerated Decision on Liability.

Date: May 13, 2011

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CERTIFICATE OF SERVICE

I, John J. McAleese, III, hereby certify that on May 13, 2011, I served a copy of **Respondent's Memorandum in Opposition to Complainant's Motion for Accelerated Decision on Liability** and supporting documents, via e-mail and Federal Express on the following:

Mark A.R. Chalfant, Esquire
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John J. McAleese, III

Exhibit A

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

IN THE MATTER OF: Elementis Chromium Inc. f/k/a Elementis Chromium, L.P., Respondent.	)))))))))	Docket No. TSCA-HQ-2010-5022

SWORN STATEMENT OF JOEL BARNHART, PH.D.

I, Joel Barnhart, Ph.D., do hereby state the following:

1. I am currently Vice President – Technical for Elementis Chromium Inc. ("Elementis Chromium"). I have held this position since 1988.

2. I received a Bachelor of Science degree from University of Texas in 1968 and a Doctorate degree in Physical Chemistry from the University of Colorado at Boulder in 1976.

3. Elementis Chromium is a manufacturer of chromium chemical products, including chromic oxide, chromic acid and sodium dichromate.

4. Elementis and its predecessors have been manufacturing chromium chemicals for more than 35 years.

5. In approximately 1984, I became a member of the Industrial Health Foundation ("IHF") Chromium Chemicals Health and Environmental Committee as the representative of American Chrome & Chemicals (now known as Elementis Chromium). I was a member of the IHF Chromium Chemicals Health and Environmental Committee from 1984 until 2003 when IHF was dissolved in bankruptcy.

6. Bayer AG and Occidental Chemical Corporation were also members of the IHF Chromium Chemicals Health and Environmental Committee during the entire time of my membership.

7. In 1998, the IHF Chromium Chemicals Health and Environmental Committee initiated an epidemiology study involving two chromium chemicals manufacturing plants located in the United States (Castle Hayne, North Carolina and Corpus Christi, Texas), two chromium chemicals manufacturing plants located in Germany (Leverkusen and Uerdingen) and one chromium chemicals manufacturing plant in the United Kingdom (Eaglescliffe, England).

8. The IHF Chromium Chemicals Health and Environmental Committee's purpose in commissioning the epidemiology study was to conduct a large study to better assess and understand the cancer risk associated with exposure to hexavalent chromium at the facilities involved in the study. Applied Epidemiology Inc. (which later became part of ENVIRON International Corporation) was contracted to undertake this work.

9. On July 24, 1998, the chair of IHF Chromium Chemicals Health and Environmental Committee, Bruce Norman, wrote to the federal Occupational Safety and Health Administration ("OSHA"), the federal Environmental Protection Agency and other regulatory bodies informing them of the initiation of the study.

10. In 1999, it became apparent that the data from the Eaglescliffe, England plant would not be compiled in time to be included in the study, so it was eliminated from the study.

11. In early 2002, Applied Epidemiology provided a draft of the report on the study to the IHF Chromium Chemicals Health and Environmental Committee. Applied Epidemiology

also provided draft copies to James Stewart of Harvard University, Harvey Checkoway of the University of Washington and Edwin van Wijingaarden of the University of North Carolina.

12. The final report of the study was presented to the IHF Chromium Chemicals Health and Environmental Committee on October 15, 2002 by Dr. Kenneth Mundt of Applied Epidemiology. Dr. Mundt reported to the IHF Chromium Chemicals Health and Environmental Committee that the results of the study had been presented at the EPICOH international conference on Epidemiology in Barcelona, Spain in the previous month.

13. Before the October 15, 2002 meeting of the IHF Chromium Chemicals Health and Environmental Committee and at the meeting, the IHF Chromium Chemicals Health and Environmental Committee discussed with Dr. Mundt the proposition that the study be divided into parts for publication since the German exposure levels were significantly higher and the data was primarily urinary chromium measurements, while the US exposure levels were lower and based on air sampling data. At the October 15, 2002 meeting, the IHF Chromium Chemicals Health and Environmental Committee discussed the possibility of dividing the study into three parts consisting of one paper on the study of the German plants, one paper on the study of the United States plants and a third paper on the exposure assessment methodology utilized in the study. The IHF Chromium Chemicals Health and Environmental Committee also discussed the complications and problems associated with correlating urinary chromium measurements with air sampling data.

14. After the October 15, 2002 IHF Chromium Chemicals Health and Environmental Committee meeting, it was my belief that the results of the study did not indicate a previously unknown substantial risk associated with exposure to hexavalent chromium.

15. When I received the draft Report in early 2002, I compared the results in the draft Report to the results reported by the 2000 EPA-sponsored study authored by Dr. Herman Gibb and others (the "Gibb Study").

16. The only information from both of these studies that reasonably supports a conclusion that hexavalent chromium presents a "substantial risk of injury to health" is that persons subject to higher exposure levels have an increased incidence of lung cancer.

17. These findings could lead to the conclusion that high levels of exposure to hexavalent chromium causes increased risk of lung cancer.

18. As the Gibb Study had already identified this potential risk, I concluded that the Report did not need to be provided to EPA pursuant to Section 8(e) of the Toxic Substances Control Act ("TSCA").

19. In 2003, IHF went bankrupt and disbanded, and Applied Epidemiology was acquired by ENVIRON International Corporation.

20. The IHF Chromium Chemicals Health and Environmental Committee did not meet again after the October 15, 2002 meeting.

Joel Barnhart
JOEL BARNHART, PH.D.

Sworn to and subscribed
before me this 11 day
of May, 2011.

Michelle Rene Moore
NOTARY PUBLIC

My commission expires:

NOTARY PUBLIC STATE OF TEXAS
MICHELLE RENE MOORE
My Commission Expires
February 2, 2015

Exhibit B

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

IN THE MATTER OF:	)	Docket No. TSCA-HQ-2010-5022
Elementis Chromium Inc. f/k/a Elementis Chromium, L.P.,	)	
Respondent.	)	

SWORN STATEMENT OF KENNETH A. MUNDT, PH.D.

I, Kenneth A. Mundt, Ph.D., do hereby state the following:

1. I am a Principal of ENVIRON International Corporation ("ENVIRON").

2. I have a Ph.D. in Epidemiology from the University of North Carolina at Chapel Hill.

3. I was a Principal of Applied Epidemiology, Inc. ("Applied Epidemiology ") until November 1, 2003 when Applied Epidemiology merged into ENVIRON.

4. In 1998, the IHF Chromium Chemicals Health and Environmental Committee initiated an epidemiology study involving two chromium chemicals manufacturing plants located in the United States (Castle Hayne, North Carolina and Corpus Christi, Texas), two chromium chemicals manufacturing plants located in Germany (Leverkusen and Uerdingen) and one chromium chemicals manufacturing plant in the United Kingdom (Eaglescliffe, England) (the "IHF Plant Study").

5. The IHF Chromium Chemicals Health and Environmental Committee's purpose in commissioning the IHF Plant Study was to conduct a large study to better assess and understand the cancer risk associated with exposure to hexavalent chromium at the facilities involved in the IHF Plant Study. Applied Epidemiology was contracted to undertake the IHF Plant Study.

6. In 1999, it became apparent that the data from the Eaglescliffe, England plant would not be compiled in time to be included in the IHF Plant Study, so it was eliminated from the IHF Plant Study.

7. One significant challenge of the IHF Plant Study was that worker exposure in the US plants had been measured by personal air monitors, while the primary measure of exposure in the German plants was through analysis of chromium in the urine of the workers.

8. In order for Applied Epidemiology to analyze the entire data set as one, it had to create a conversion factor to convert air concentrations measured by the personal air monitors to urine chromium levels. This required Applied Epidemiology to make some very substantial assumptions.

9. After making such assumptions, Applied Epidemiology came up with a single conversion factor that it used to convert all of the air monitoring exposure valuations to urine chromium levels.

10. Applied Epidemiology then broke the cohort into four different groups based on relative exposure levels. For each exposure group, Applied Epidemiology compared the number of persons within each group who had contracted lung cancer with the number of people that

would be expected to contract lung cancer in the group based on statistics from the general population in the locals where the plants were situated.

11. The highest exposure group, the persons with exposures of $\geq$200 μg/L, contained a total of 117 workers. Of this number of workers, there were 12 cases of lung cancer. When compared with the number of cases that would be expected in the general population based on historical reporting, 5.72 expected cases, Applied Epidemiology concluded that number of actual cases of lung cancer in this group indicated that there was an elevated risk of contracting lung cancer exhibited by this group.

12. None of the other groups showed a statistically significant increase in the number of cancer cases. Specifically, the exposure group 0-39.9 μg/L had 4 reported cases of lung cancer, with 6.37 expected,[1] the exposure group 40-99.9 μg/L, had 4 reported cases of lung cancer, with 4.20 expected, and the exposure group 100-199.9 μg/L, had 5 reported cases, with 5.30 expected.

13. The results of the IHF Plant Study did not identify any substantial risks associated with hexavalent chromium that had not been previously reported. Numerous prior studies, including the 2000 EPA-funded study authored by Dr. Herman Gibb and others, had identified the same substantial risks of exposure to hexavalent chromium that were identified in the IHF Plant Study.

14. In early 2002, I provided a draft of the report on the IHF Plant Study to the IHF Chromium Chemicals Health and Environmental Committee. The report was entitled the

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[1] The number of expected cases for this exposure group was incorrectly reported to be 2.97 in the September 27, 2002 version of report on the IHF Plant Study. An amended version of the report was issued in April 2003 after this error was found. The April 2003 version of the report correctly reported the expected number of cases of lung cancer to be 6.37.

"Collaborative-Cohort Mortality Study of Four Chromate Production Facilities, 1958-1998, Final Report" (the "Report"). I also provided draft copies of the Report for review and comment to the Scientific Advisory Board ("SAB") convened by Applied Epidemiology in connection with the study. The SAB consisted of professors James Stewart, Ph.D. of Harvard University, Harvey Checkoway, Ph.D. of the University of Washington and Edwin van Wijingaarden, Ph.D. of the University of North Carolina.

15. I e-mailed the "final" Report dated September 27, 2002 to the members of the IHF Chromium Chemicals Health and Environmental Committee on October 8, 2002.

16. I presented, in person, the results of the IHF Plant Study at the IHF Chromium Chemicals Health and Environmental Committee meeting on October 15, 2002.

17. During the October 15, 2002 meeting, I reported to the IHF Chromium Chemicals Health and Environmental Committee that I had presented the results of the IHF Plant Study at the EPICOH international conference on Epidemiology in Barcelona, Spain in September 2002. This conference is a periodic gathering of the world's preeminent occupational epidemiologists.

18. Before the October 15, 2002 meeting of the IHF Chromium Chemicals Health and Environmental Committee, and at the meeting, the IHF Chromium Chemicals Health and Environmental Committee discussed with me the proposition that the Report be divided into parts for publication since the German exposure levels were significantly higher and the data were primarily urinary chromium measurements, while the US exposure levels were lower and based on air sampling data.

19. The IHF Chromium Chemicals Health and Environmental Committee also discussed the complications and problems associated with correlating urinary chromium measurements with air sampling data. I confirmed with the IHF Chromium Chemicals Health and Environmental Committee that similar concerns and issues about combining the cohorts had been discussed with me by peers at the September 2002 EPICOH conference.

KENNETH A. MUNDT, PH.D.

Sworn to and subscribed
before me this 11th day
of May, 2011.

NOTARY PUBLIC

My commission expires: 3/1/2013

ABIGAIL R. LAVALLEY
MY COMMISSION EXPIRES MARCH 1, 2013
COMMONWEALTH OF MASSACHUSETTS
NOTARY PUBLIC

Exhibit C

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

IN THE MATTER OF: Elementis Chromium Inc. f/k/a Elementis Chromium, L.P., Respondent.	))))))))	Docket No. TSCA-HQ-2010-5022

AFFIDAVIT OF HERMAN J. GIBB, Ph.D., M.P.H.

1. I, Herman J. Gibb, Ph.D., M.P.H., am President of Tetra Tech Sciences, a health and environmental risk assessment company consulting company in Arlington, Virginia.

2. I have a Ph.D. in epidemiology (Johns Hopkins University School of Hygiene and Public Health, 1989) and an M.P.H. in Environmental Health (University of Pittsburgh Graduate School of Public Health, 1974).

3. I am the Chairman of the Chemical Task Force of the World Health Organization's Food borne Epidemiology Reference Group and a member of the Pool of Scientific Advisors of the European Commission (EC) appointed by the EC's Health and Consumers Directorate-General.

4. I am a Lecturer in Environmental and Occupational Health at the George Washington University School of Public Health at the George Washington University School of Public Health and Health Services.

5. Prior to joining Tetra Tech Sciences in January 2004, I served in several positions at the National Center for Environmental Assessment at the U.S. Environmental Protection

Agency ("EPA") including Associate Director for Health, Assistant Center Director, and staff epidemiologist. I was employed at EPA from October 1974 until January 2004.

6. While at EPA, I provided consultation to several foreign governments particularly on issues related to metals and served on a number of Task Groups and Review Boards of the International Program on Chemical Safety (IPCS).

7. I am the author or co-author of numerous publications on epidemiology and health risk assessment. I have been the speaker, including the keynote speaker, at various international symposia on health risk assessment. I was co-author of the International Program on Chemical Safety's Environmental Health Criteria Document, *Principles for the Assessment of Risks to Human Health from Exposure to Chemicals* and EPA's *An Examination of EPA's Risk Assessment Principles and Practices*. I received EPA's Gold Medal for Exceptional Service for my analysis of the epidemiologic studies on arsenic, EPA's Award for September 11 Activities, World Trade Center Particulate Matter Toxicological Assessment Team, and numerous EPA bronze medals for my risk assessment work.

8. I am the senior author of two journal articles describing an epidemiologic study of workers at a chromate production facility in Baltimore, MD (Gibb et al. 2000a, Gibb et al. 2000b). The study was conducted and the papers were published while I was an employee at EPA, and EPA funded this study. Gibb et al. (2000a) describes the analysis of lung cancer risk among the workers; Gibb et al. (2000b) describes clinical irritation among the workers. For the work on the study of lung cancer risk, I was honored by EPA's Scientific and Technological Achievement Award. The citation for the award states that the study was the "Most detailed and significant study of the lung and clinical irritation risks from chromium exposure ever conducted." The study became a critical part of the Occupational Safety and Health

Administration's (OSHA) Permissible Exposure Limit (PEL) on hexavalent chromium. I was asked by OSHA to be the lead witness at OSHA's public hearing on the proposed PEL in 2005. The PEL was finalized in 2006. The National Institute of Occupational Safety and Health made Gibb et al. (2000a) the basis of its Recommended Exposure Limit (REL) on hexavalent chromium. The REL was proposed in September 2008 as part of its "Criteria Document Update – Occupational Exposure to Hexavalent Chromium" and I was invited to a public hearing in Cincinnati to serve as a peer reviewer on the proposed document. The document is expected to be released in 2011.

9. The *"Collaborative-Cohort Mortality Study of Four Chromate Production Facilities, 1958-1998, Final Report"* prepared by Applied Epidemiology dated September 27, 2002 (hereafter referred to as Mundt et al. 2002) provides no new information with respect to the respiratory risk of hexavalent chromium and does not add to the knowledge base on the lung cancer risk from occupational exposure to hexavalent chromium.

10. It has been known for at least 60 years that exposure to hexavalent chromium increases the risk of lung cancer. EPA contends that the Mundt et al. (2002) report fills a critical gap for "modern" chromium facilities using low-lime or no-lime kiln manufacturing. Low lime or no lime processing reduces or eliminates exposure to calcium chromate. At one time, it was theorized that calcium chromate was the hexavalent chromium compound responsible for the increased respiratory cancer risk in chromate production facilities. That theory was dismissed by EPA (1984) over a quarter of a century ago in favor of the theory that all hexavalent chromium compounds should be considered carcinogenic. The position that all hexavalent chromium compounds should be considered carcinogenic is shared by multiple federal and international

health risk assessment authorities (NIOSH 2008, OSHA 2006, IARC 1997, Health Canada 1994, NTP 2010).

11. With respect to the respiratory cancer risk at "modern" facilities, EPA has never considered there to be a threshold to the carcinogenic risk from hexavalent chromium, and since 1984 has used a *linear* model to estimate the lung cancer risk expected from low dose exposure (U.S. EPA 1984; U.S. EPA 2010). In other words, regardless of how "modern" a facility is, EPA, as well as others in the scientific community (NIOSH 2008; OSHA 2006), considers any hexavalent chromium exposure to present some lung cancer risk.

12. Furthermore, the Baltimore facility studied by Gibb et al. (2000a) could also be considered "modern." Gibb et al. (2000a) is the basis of the OSHA Permissible Exposure Limit on hexavalent chromium and the basis of the proposed NIOSH Recommended Exposure Limit. The Baltimore facility studied by Gibb et al. (2000a) was rebuilt in 1950 (a chromium production plant had existed at that location since the 19th century), and major modifications were made in 1960 to improve the industrial hygiene.

13. It has been EPA's position for over a quarter of a century that increasing exposure to all hexavalent chromium is associated with increasing lung cancer risk.

Washington, D.C.

Subscribed and Sworn to before me this 13th day of May, 2011

Herman J. Gibb

HERMAN J. GIBB, Ph.D., M.P.H.

Sworn to and subscribed before me this 13th day of May, 2011

Tricia M. Farringer

Notary Public

TRICIA M. FARRINGER
NOTARY PUBLIC DISTRICT OF COLUMBIA
My Commission Expires Oct. 31, 2013

Exhibit D

Lung Cancer Among Workers in Chromium Chemical Production

Herman J. Gibb, PhD,[1*] Peter S. J. Lees, PhD,[2] Paul F. Pinsky, PhD,[3] and Brian C. Rooney, MS[2]

Background *An elevated risk of lung cancer among workers in chromate production facilities has previously been reported. This excess risk is believed to be the result of exposure to hexavalent chromium. There have been mixed reports about whether trivalent chromium exposure is also associated with an excess lung cancer risk. Previous studies of measured hexavalent chromium exposure and lung cancer risk have not examined cigarette smoking as a risk factor.*

Methods *A cohort of 2,357 workers first employed between 1950 and 1974 at a chromate production plant was identified. Vital status of the workers was followed until December 31, 1992. Work histories of cohort members were compiled from the beginning of employment through 1985, the year the plant closed. Annual average exposure estimates, based on historical exposure measurements, were made for each job title in the plant for the years 1950–1985. These exposure estimates were used to calculate the cumulative hexavalent chromium exposure of each member of the study population. Following closure of the plant, settled dust samples were collected and analyzed for hexavalent and trivalent chromium. The trivalent/hexavalent concentration ratios in each plant area were combined with historic air-sampling data to estimate cumulative trivalent chromium exposure for each individual in the study cohort. Smoking status (yes/no) as of the beginning of employment and clinical signs of potential chromium irritation were identified from company records.*

Results *Cumulative hexavalent chromium exposure showed a strong dose–response relationship for lung cancer. Clinical signs of irritation, cumulative trivalent chromium exposure, and duration of work were not found to be associated with a risk of lung cancer when included in a proportional hazards model with cumulative hexavalent chromium exposure and smoking. Age-specific data on cumulative hexavalent chromium exposure, observed and expected numbers of lung cancer cases, and person-years of observation are provided.*

Conclusion *Cumulative hexavalent chromium exposure was associated with an increased lung cancer risk; cumulative trivalent chromium exposure was not. The excess risk of lung cancer associated with cumulative hexavalent chromium exposure was not confounded by smoking status. The current study offers the best quantitative evidence*

[1]U.S. Environmental Protection Agency, Washington, DC

[2]The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD

[3]U.S. Environmental Protection Agency (Currently with the National Cancer Institute)

Contract grant sponsor: U.S. Environmental Protection Agency; Contract grant number: CR822033-01

Institutions At Which The Work Was Performed: National Center for Environmental Assessment, U.S. Environmental Protection Agency, Ariel Rios Building, 1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460; The Johns Hopkins University School of Hygiene and Public Health, 615 N. Wolfe Street, Baltimore, MD 21205

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to date of the relationship between hexavalent chromium exposure and lung cancer. Am. J. Ind. Med. 38:115–126, 2000. *Published 2000 Wiley-Liss, Inc.*†

KEY WORDS: hexavalent chromium; chromate; lung cancer; smoking; trivalent chromium; exposure response

INTRODUCTION

An excess risk of bronchogenic carcinoma was reported among workers in the German chromate-producing industry prior to World War II, but the conclusion that chromates should be considered as carcinogenic was not generally accepted by the medical profession in the United States until after the war [Public Health Service, 1951]. Following the war, several studies of the lung cancer risk among chromate production workers in the United States reported that an increased lung cancer risk did indeed exist [Machle and Gregorius, 1948; Baetjer, 1950; and Mancuso and Hueper, 1951]. As a result of these reports and additional reports from other countries, the U.S. Public Health Service (PHS) was requested to conduct an evaluation of the lung cancer risk in the U.S. chromate production industry and to make recommendations with respect to potential medical and engineering control measures. In 1951, the PHS report on the *Health of Workers in the Chromate Producing Industry* was issued. It concluded, based on environmental investigations and medical examinations at six chromate production plants and on a study of the mortality and morbidity experience of male members of "sick benefit associations" in seven chromate-producing plants that workers in the American chromate production industry did have an excess risk of bronchogenic cancer. The report further concluded that while chromium in some form was implicated, the exact causative agent had not yet been determined.

In 1980, the International Agency for Research on Cancer concluded that "chromium and certain chromium compounds" were known human carcinogens [IARC, 1980]. The U.S. EPA [1984], using IARC [1980] guidelines of classification, concluded that hexavalent chromium compounds were known human carcinogens but that trivalent chromium compounds could not be classified. IARC [1987] concluded that hexavalent chromium was a known human carcinogen and that metallic and trivalent chromium could not be classified. IARC [1990], ATSDR [1993] and Health Canada [1994] all indicated that an increased risk of lung cancer has been consistently demonstrated in studies of the chromate production, chrome plating, and chrome pigment production industries.

The EPA health assessment document [1984] estimated the excess lifetime lung cancer risk due to air containing 1 $\mu g/m^3$ hexavalent chromium based on the results reported by Mancuso [1975]. The Mancuso study also formed the basis of quantitative estimates of lung cancer risk by the Government of Canada [1994] and by K.S. Crump Division [1995]. The EPA document noted several limitations in the Mancuso data for exposure–response assessment of the lung cancer risk of hexavalent chromium: (1) risk was presented by exposure group and age for total chromium exposure but not for hexavalent chromium exposure; (2) no smoking data were available on the workers; and (3) the industrial hygiene survey that was relied on by Mancuso for his exposure estimates was done in 1949, while Mancuso's cohort was defined as having begun employment between 1931 and 1937. The current study has advantages over the Mancuso study for quantitative assessment of the lung cancer response to hexavalent chromium for a variety of reasons which will be discussed below.

As indicated above, the evidence of carcinogenicity of trivalent chromium is generally considered to be inadequate. Mancuso [1975], however, concluded that exposure to trivalent chromium was associated with an increased risk of lung cancer and maintained this position in his 1997 update of the study [Mancuso, 1997a]. Although airborne concentrations of trivalent chromium are greater than hexavalent chromium in chromate production facilities, these two exposure measures are generally correlated, and it is difficult to separate the effects of the two. The current study evaluates the risk of lung cancer from both trivalent and hexavalent chromium exposure.

MATERIALS AND METHODS

The cohort for the current study is based on that identified by Hayes et al. [1979] at a chromate production plant in Baltimore, MD. Hayes et al. identified 4,217 workers newly employed between January 1, 1945 and December 31, 1974. The cohort defined by Hayes et al. excluded workers employed less than 90 days (N = 1,915), women (N = 160), and those with unknown length of employment (N = 24), work history (N = 16), and/or age (N = 1). The resulting study group of 2,101 persons included 1,803 hourly employees and 298 salaried employees. The current study excluded those in the Hayes et al. cohort who began work before August 1, 1950 (N = 734) because on that date, the construction of a new mill and roast and bichromate plant was completed and extensive exposure information began to be collected. It was also decided to include workers in the current study who worked less than 90 days but began employment after August 1, 1950 (N = 990), to expand the size of the low exposure group.

The resulting group of 2,357 males constituted the cohort for this study.

In the Hayes et al. study, the vital status of the cohort was followed through July 1977 by a variety of means (e.g., Social Security Administration, Department of Motor Vehicles, voter registration lists, etc.). The current study utilized the National Death Index [McMahon, 1983] to identify deaths between January 1, 1979 and December 31, 1992. The National Death Index began on January 1, 1979 and thus was not available to Hayes et al. at the time of their study. Between July 1977, the end of follow up of the Hayes study, and December 31, 1978, the current study utilized Social Security data to determine deaths among cohort members. Death certificates were requested from the states where the former employees died. Causes of death were coded to the 8th Revision of the ICDA. Person-years of observation were calculated from beginning of employment until death or December 31, 1992, which was the last date to which the National Death Index was queried for the current study. Work histories on all the workers were updated through July 1985 when operations at the plant ceased. The work histories in the Hayes et al. study were available through 1974.

Smoking status (yes/no) as of beginning of employment was identified for 2,137 (93.3%) of the cohort of 2,357 from company medical records. Data on cigarette, pipe, and cigar smoking were included.

Exposure

The hexavalent chromium exposure of each member of the cohort was estimated for the duration of their employment at the chromate production facility. Exposure estimates were assigned by job title and based on approximately 70,000 contemporary measurements of airborne hexavalent chromium concentration spanning the study period. These exposure estimates were merged with each study member's work history to provide a profile of annual average exposures throughout their period of employment at the chromate production facility.

Immediately following the completion of the new production facility in 1950, a program of routine air sampling for hexavalent chromium was undertaken. The air sampling program was highly unusual in that it was based on a written document that clearly specified the objectives of the program and strategies for air sampling. Historically, and to a large extent continuing to the present day, industrial hygiene air sampling has focused on the identification of problems and as a result has been a biased measure of the entire worker population exposure in a facility. According to the facility's program, air sampling was undertaken in order to characterize "typical/usual exposures" of workers. This point is particularly relevant to the conduct of this epidemiologic study in that the resulting exposure estimates can be reasonably assumed to represent average exposures.

During the period from 1950 to 1961, airborne dust samples were collected using high volume air sampling pumps and impingers with the sampling wand held by the industrial hygienist in the worker's breathing zone. The resulting exposure estimates were, of necessity, the result of short-term (tens of minutes) samples. Beginning in the mid-1960s a system of exposure estimation based on 24-hour routine measurements at fixed-site monitors throughout the facility combined with routine observation of how much time job titles spent in the vicinity of each of these monitors was instituted. In this system, approximately 20 RAC tape air samplers (Research Appliance Co., Allison Park, PA) were rotated through 154 fixed sites, representing discrete "exposure zones," in and around the production complex. Twenty-four 1-hour air samples were collected per day at each sampling location. (After 1979, the number of fixed sites and associated exposure zones was reduced to 27 and sampling was reduced to eight 3-hour samples at each location.) Direct daily observations by a plant employee of the location of persons (specified by job titles) with respect to these samplers were used to calculate job title-based exposure estimates by multiplying the fractional person-time spent by given job title in each sampling zone and summing these fractions. This system remained in use until 1985 when the plant closed. Beginning in 1977, this system was supplemented by routine full-shift personal sample collection, again based on job title, using NIOSH standard method P and CAM 169 [NIOSH, 1974]. Despite different dust collection methods throughout the period of this study, the sample analytical method remained essentially constant, using minor variants of the s-diphenylcarbazide colorimetric method; all analyses were conducted by an in-house laboratory.

The first step in the exposure estimation process was to convert all measurements to a common basis. During different time periods, airborne contaminant concentrations were presented in terms of mass of Cr and CrO_3; for this study all measurements were converted to CrO_3. Measurements used in this report are thus mg CrO_3/m^3, the metric used by the U.S. Occupational Safety and Health Administration [OSHA, 2000] in its current Permissible Exposure Limit for chromic acid and chromates. Note that the current Threshold Limit Value for soluble chromium published by the American Conference of Governmental Industrial Hygienists [1999] is specified in terms of mass of Cr.

Exposure estimates derived from the area sampling system described above were adjusted to an equivalent personal exposure estimate using job-specific ratios of the mean area and personal sampling exposure estimates for the period 1978–1985 when both systems were in use. The comparison of exposure estimates derived from area and personal samples showed no significant differences (i.e., ratio approximately 1) for approximately two-thirds of the job titles with a sufficient number of samples to make this comparison. For the remaining job titles, virtually all of which were associated with a significant point source of contamination and including job titles such as "soda packer" and "chromic acid packer," the area sampling method was found to significantly underestimate personal exposure estimates and were, thus, adjusted by the ratio of the two.

Exposure estimates were used to construct a job exposure matrix (JEM) displaying annual average exposure for each job title. The JEM included entries for annual average exposure estimates for 114 job titles and 36 years. (As jobs titles were eliminated and consolidated over the years, it was not necessary to provide exposure estimates for all cells in the matrix.) Wherever air sampling data were available, the annual average concentration was entered directly into the JEM. Data were virtually complete for most job titles for the years 1971–1985 and fairly complete for fewer job titles for the years 1950–1956 and 1960–1961. Although there is indirect evidence that air sampling was conducted in the interim periods, exposure measurements could not be located for these years.

Exposures were modeled for the cells in the JEM without direct measures. A protocol for utilizing the existing data to model missing cells in the matrix was developed and followed to provide a uniform approach to estimate historic exposures from existing exposure data. Several exposure estimation methods were used. The primary estimator for missing data was based on a simple model using the ratio of the measured exposure for a job title to the average of all measured job titles in the same department. A hierarchy was established in which data available for the closest year were used. This approach was found to produce stable and robust estimates of exposure. For periods in which there were extensive missing data, primarily the data gap in the 1960s, exposures were estimated through a simple straight-line interpolation between years with known exposures.

Airborne trivalent chromium concentrations were never measured in the facility. Using a method similar to that employed by Mancuso [1975, 1997a] to estimate the hexavalent chromium exposures, airborne trivalent dust concentrations were estimated through the use of measured airborne hexavalent chromium concentrations and the ratio of hexavalent chromium concentration to trivalent chromium concentration in settled dust in the facility. This approach is based on the assumptions that the Cr^{+3}:Cr^{+6} ratio of the settled dust collected was representative of the ratio when the facility was in operation, that the Cr^{+3}:Cr^{+6} ratio in respirable airborne dust was the same as that in the settled dust, and that this ratio did not change from 1950 to 1985. There is no way to verify or refute any of these assumptions.

Seventy-two composite settled dust samples were collected at or near 26 of the 27 fixed-site air monitoring stations approximately 3 years after the facility closed. The facility had been sealed from the ambient environment with very limited access during this period. The dust samples were extracted and analyzed for hexavalent chromium content using ion chromatography; trivalent chromium content was determined through inductively coupled plasma spectroscopic analysis of the residue. The Cr^{+3}:Cr^{+6} ratio was calculated for each area corresponding to the air sampling zones and the measured hexavalent chromium air concentration adjusted based on this ratio. The mean Cr^{+3}:Cr^{+6} ratio was 6.2 and ranged from 0.02 to 77 across these zones (two zones with only trace Cr^{+6} were excluded from the data summary). As described previously, worker exposures were calculated for each job title, and weighted by the fraction of time spent in each air monitoring zone. The Cr^{+3}:Cr^{+6} ratio was derived in this manner for each job title based on the distribution of time spent in exposure zones in 1978. Hexavalent chromium exposure estimates in the JEM were multiplied by this ratio to estimate trivalent chromium exposures. The resulting mean Cr^{+3}:Cr^{+6} ratio for individual job titles was 17 and ranged from 1.2 to 64. A separate JEM for trivalent chromium exposures was thus constructed and used in conjunction with subject work histories to provide individual profiles of trivalent chromium exposure for analysis.

Statistical Methods

Observed-to-expected mortality ratios were calculated for various causes of death for whites and nonwhites and the total cohort. Expected deaths were calculated using age-, calendar-, and race-specific U.S. mortality rates. The expected lung cancer deaths were a total of the expected lung cancer deaths for whites, nonwhites, and those with unknown race. The expected lung cancer deaths for those with unknown race was estimated from what would be expected if they had a race distribution similar to those for whom race was known.

Observed-to-expected ratios of lung cancer mortality were calculated for whites, nonwhites, race unknown, and the entire cohort by cumulative exposure quartile. Cumulative exposure was calculated in a dynamic fashion. In other words, for each person at any given age, cumulative exposure was counted as the exposure up to that age, lagged 5 years (i.e., only exposure occurring 5 years before a given age was counted). Although cumulative exposure was calculated in a dynamic fashion, the cut points for the quartiles are those that divide the persons in the cohort into four equal groups based on their cumulative exposure at the end of their working history. Expected deaths were estimated using race-, age-, and calendar year-specific mortality rates for the State of Maryland using OCMAP

[Marsh and Preininger, 1980]. Maryland, rather than U.S. rates, were used for this part of the analysis since Maryland has one of the highest lung cancer mortality rates in the U.S. [Riggan et al., 1983]. The lung cancer rates in Maryland are heavily influenced by the rates in Baltimore City which has even higher lung cancer rates than the State of Maryland (and is where the chromate production plant was located), but the Maryland rates were chosen because many of the deaths occurred in Maryland outside of Baltimore City (16%) and many occurred in other states (39%). A table of age-specific observed and expected lung cancer deaths and the person-years of observation by cumulative hexavalent chromium exposure was developed for the total cohort, again estimating cumulative exposure in a dynamic fashion and lagging exposures 5 years.

Proportional hazards models [Cox, 1972] using age as the time variable and cumulative exposure as a time-varying covariate were used to assess the relationship of chromium exposure to the risk of lung cancer. Various exposure metrics [e.g., cumulative exposure with different lag periods, average exposure (cumulative exposure/duration of work) with different lag periods, duration of work, etc.] were evaluated. Final models were developed for each exposure measure using a forward step-wise procedure with a P-value for entry and exit of 0.05; P-values were derived using the likelihood ratio test. The variables considered for inclusion were race (white/nonwhite/unknown), calendar decade, and cigarette smoking, in addition to the exposure measure.

The association of lung cancer with 10 different clinical findings of potential chromium irritation observed in the study cohort (irritated nasal septum, ulcerated nasal septum, perforated nasal septum, bleeding nasal septum, irritated skin, ulcerated skin, dermatitis, burn, conjunctivitis, perforated eardrum) was examined in 2 × 2 tables and by 10 different Cox proportional hazards models. These clinical findings were identified by routine examination and through complaints reported by the individual to the health clinic at the plant. All findings were diagnosed by a physician. In the Cox model, the clinical finding was time-varying in that the variable was treated as 0 for the person-years prior to the first onset of the finding and 1 afterward.

RESULTS

There was a total of 70,736 person-years of observation. A summary of selected causes of death is reported in Table I. These causes were selected from 55 causes of death that were examined because either white, nonwhite, unknown, or the total showed a significant excess or deficit risk. Deaths from all cancers, cancer of the lung, mental disease, psychoneurotic, and personality disorders, and suicide were significantly elevated in the total cohort. Deaths from cancer of the prostate and arteriosclerotic heart disease were elevated in the total cohort but of borderline significance. There was a deficit of deaths from accidents that was of borderline significance among nonwhites; this deficit was not statistically significant among whites or race unknown or in the total cohort.

Table II provides a description of the entire cohort, the lung cancer cases, and the noncases by selected continuous variables.

There were two categorical variables used in the analyses—race and smoking. The cohort included 1,205 (51%) whites, 848 (36%) nonwhites, and 304 (12.9%) race unknown. Seventy-one (58%) of the 122 lung cancer cases occurred in whites, 47 (39%) in nonwhites, and 4 (3%) in race unknown. A comparison by race of selected continuous variables is found in Table III. A description of the smoking status of the cohort is provided in Table IV. As indicated previously, smoking status was reported as of date of first employment.

TABLE I. Observed/Expected Ratios for Selected Causes of Death; Chromium Chemical Production Workers, USA[a]

	White			Nonwhite			Race unknown[b]			Total		
Cause of death	**O**	**O/E**	**95% CI**	**O**	**O/E**	**95% CI**	**O**	**O/E**	**95% CI**	**O**	**O/E**	**95% CI**
All causes	472	1.09	1.00–1.20	323	1.02	0.91–1.14	60	1.00	0.76–1.29	855	1.06	0.99–1.13
All cancers	120	1.14	0.94–1.36	99	1.44	1.17–1.75	16	1.21	0.69–1.97	235	1.25	1.10–1.42
Arteriosclerotic heart disease	154	1.07	0.91–1.26	84	1.32	1.05–1.63	14	1.05	0.57–1.76	252	1.14	1.01–1.29
Cancer of lung	71	1.86	1.45–2.34	47	1.88	1.38–2.51	4	0.83	0.22–2.13	122	1.80	1.49–2.14
Cancer of prostate	5	0.71	0.23–1.67	11	2.03	1.01–3.63	0	0	0–5.56	16	1.22	1.00–1.98
Mental, psychoneurotic, and personality disorders	8	2.44	1.05–4.82	10	1.78	0.85–3.27	6	5.61	2.05–12.21	24	2.41	1.54–3.58
Suicide	9	0.91	0.42–1.73	9	2.94	1.34–5.68	3	1.90	0.32–5.54	21	1.66	1.06–2.46
Accidents	25	0.99	0.64–1.45	15	0.60	0.34–0.99	2	0.33	0.04–1.21	42	0.75	0.54–1.01

[a]Expected deaths are based on age-, race-, and calendar-year specific rates for the USA.

[b]The expected deaths for those with race unknown was estimated from what would be expected if they had a race distribution similar to those for whom race was known.

TABLE II. Description of Entire Cohort by Cumulative Hexavalent Chromium Exposure, Cumulative Trivalent Chromium Exposure, Years of Work at the Plant, Age at Hire, Years of Follow up, and Calendar Year of Hire [N (Total Group) = 2,357, N (Lung Cancer Cases) = 122, N (Noncases) = 2,235]; Chromium Chemical Production Workers, USA

Statistic \ Variable	Cumulative hexavalent chromium exposure (mg/m^3-years)	Cumulative trivalent chromium exposure (mg/m^3-years)	Work years	Years of follow up	Age at hire	Calendar year of hire (19XX)
Mean						
Total group	0.134	1.98	3.1	30.0	30.2	57.7
Lung cancer cases	0.290	3.57	5.3	27.9	33.3	53.5
Noncases	0.125	1.90	3.0	30.1	30.0	58.0
Standard deviation						
Total group	0.357	5.28	6.5	9.6	7.5	7.7
Lung cancer cases	0.620	7.39	9.1	8.5	8.8	4.1
Noncases	0.335	5.13	6.3	9.7	7.4	7.8
Median						
Total group	0.009	0.11	0.39	31.2	28.6	54
Lung cancer cases	0.016	0.22	0.84	28.9	31.6	53
Noncases	0.009	0.11	0.41	31.3	28.5	54
Min/max						
Total group	0/5.3	0/64.7	0.003/37.7	0.3/42.3	16.9/62.9	50/74
Lung cancer cases	0/4.1	0/36.4	0.003/32.2	6.4/42.2	21.2/62.6	50/73
Noncases	0/5.3	0/64.7	0.003/37.9	0.3/42.4	16.9/62.9	50/74
25th percentile						
Total group	0.001	0.014	0.088	22.6	24.3	51
Lung cancer cases	0.002	0.024	0.167	22.1	26.3	51
Noncases	0.001	0.014	0.085	22.7	24.3	51
75th percentile						
Total group	0.076	0.98	2.0	38.9	34.4	65
Lung cancer cases	0.226	2.79	4.6	35.1	39.2	54
Noncases	0.072	0.94	2.0	39.2	34.2	65

TABLE III. Comparison of Mean Age at Hire, Mean Work Duration, Mean Follow-up, and Mean Cumulative Hexavalent and Trivalent Chromium Exposure By Race; Chromium Chemical Production Workers, USA

Race	Mean age at hire	Mean work duration (years)	Mean follow up (years)	Mean cumulative hexavalent chromium exposure (mg/m^3-years)	Mean cumulative trivalent chromium exposure (mg/m^3-years)
White (N = 1205)	31.4	3.3	31.6	0.13	1.88
Nonwhite (N = 848)	28.9	3.7	29.1	0.18	2.79
Unknown (N = 304)	28.6	0.6	26.4	0.03	0.28

There was a high proportion of cigarette smokers and "any smoking" among both whites (83 and 86%, respectively), nonwhites (82 and 86%, respectively), and race unknown (79 and 81%, respectively). The vast majority of the lung cancer cases occurred among cigarette smokers (116) vs. nonsmokers (4). For two lung cancer cases, the smoking status was unknown.

Table V presents the numbers of observed and expected lung cancer deaths, the observed-to-expected ratios, person-years of observation, and the mean cumulative hexavalent

TABLE IV. Smoking Status of the Cohort; Chromium Chemical Production Workers, USA

Smoking category	Smoking status: Yes	No	Unknown
Cigarette smoking	1,753 (82%)	384 (18%)	220
Any smoking (includes cigarettes, cigars, and pipes)	1,834 (86%)	307 (14%)	216

TABLE V. Observed and Expected Lung Cancer Deaths, Person-years of Observation, Observed to Expected Ratios, and Cumulative Hexavalent Chromium Exposure By Age[a]; Chromium Chemical Production Workers, USA

Range of cumulative exposure (mg CrO_3/m^3-years)		Age: 20–29	30–39	40–49	50–59	60–69	70–79	80+
0–0.00149	Observed lung cancer deaths	0	1	0	14	8	2	1
	Expected lung cancer deaths	0.018	0.39	2.50	7.56	10.79	5.00	0.88
	Person-years of observation	5,003	7,684	6,509	5,184	3,104	865	163
	Observed/expected	0	2.48	0	1.85	0.74	0.40	1.13
	Mean exposure (mg CrO_3/m^3-years)	0.00021	0.00041	0.00051	0.00053	0.00050	0.00046	0.00040
0.00150–0.0089	Observed lung cancer deaths	0	0	2	10	10	4	2
	Expected lung cancer deaths	0.001	0.18	1.97	6.09	7.85	3.25	0.44
	Person-years of observation	349	3,139	4,643	3,928	2,183	558	79
	Observed/expected	0	0	1.02	1.64	1.27	1.23	4.55
	Mean exposure (mg CrO_3/m^3-years)	0.0042	0.0043	0.0043	0.0042	0.0042	0.0039	0.0037
0.009–0.0769	Observed lung cancer deaths	0	0	3	10	11	4	2
	Expected lung cancer deaths	0.002	0.19	1.93	5.70	7.66	3.26	0.38
	Person-years of observation	457	3,520	4,732	3,720	2,128	559	78
	Observed/expected	0	0	1.56	1.75	1.44	1.23	5.27
	Mean exposure (mg/m^3-years)	0.031	0.031	0.030	0.030	0.028	0.029	0.027
0.077–5.25	Observed lung cancer deaths	0	0	8	8	18	3	1
	Expected lung cancer deaths	0.001	0.17	1.82	5.63	6.71	2.48	0.18
	Person-years of observation	200	2,874	4,294	3,663	1,926	423	29
	Observed/expected	0	0	4.41	1.42	2.68	1.21	5.43
	Mean exposure (mg CrO_3/m^3-years)	0.21	0.33	0.41	0.52	0.63	0.78	0.86

[a]Expected lung cancer deaths in this table are based on age-, race-, and calendar-year- specific rates for the State of Maryland. The expected lung cancer deaths for those with race unknown was estimated from what would be expected if they had a race distribution similar to those for whom race was known. Cumulative exposure is lagged 5 years.

chromium exposure by age category. The table has been further organized by cumulative exposure quartiles.

Table VI is an examination of lung cancer observed-to-expected ratios by race (white, nonwhite) and for the total cohort for the four cumulative hexavalent chromium exposure quartiles. For whites, the lung cancer risk increased from the first to the second quartile, leveled off in the third quartile and decreased in the fourth quartile. For nonwhites the lung cancer risk was not significantly elevated except for the fourth quartile. For those with race unknown, there were few lung cancer deaths. The total cohort, however, demonstrated a monotonic exposure–response relationship between cumulative hexavalent chromium exposure and lung cancer observed-to-expected ratio.

As indicated in the Methods section, proportional hazards models were used to assess the relationship between chromium exposure and the risk of lung cancer. Log transformation of cumulative exposure (for both cumulative trivalent chromium exposure and cumulative hexavalent chromium exposure) was found to improve the fit of the model (i.e., greater χ^2 statistic) as compared to using the untransformed exposure measure. This improvement was seen with all lag periods considered; with a 5-year lag the χ^2 increased from 35.9 to 42.1 for hexavalent chromium and

TABLE VI. Lung Cancer Observed and Expected Deaths, Person Years of Observation, and Observed-to-Expected Ratios By Race for the Four Exposure Quartiles; Chromium Chemical Production Workers, USA[a]

Cumulative hexavalent chromium exposure (mg CrO_3/m^3-years)	Race			
	White	Nonwhite	Unknown	Total
0–0.00149 Mean = 0.00045	O/E = 0.83 (95% CI = 0.47, 1.35) O = 14, E = 16.81 PY = 16,299	O/E = 1.15 (95% CI = 0.55, 2.07) O = 9, E = 7.85, PY = 8,400	O/E = 1.23 (95% CI = 0.3, 3.2) O = 3, E = 2.44 PY = 3,813	O/E = 0.96 (95% CI = 0.63, 1.38) O = 26, E = 27.1 PY = 28,512
0.0015–0.0089 Mean = 0.0042	O/E = 2.10 (95% CI = 1.31, 3.16) O = 20, E = 9.54 PY = 7,330	O/E = 0.93 (95% CI = 0.42, 1.72) O = 8, E = 8.63 PY = 5,296	O/E = 0 (95% CI = 0, 2.3) O = 0, E = 1.63 PY = 2,253	O/E = 1.42 (95% CI = 0.95, 2.01) O = 28, E = 19.80 PY = 14,879
0.009–0.0769 Mean = 0.030	O/E = 2.11 (95% CI = 1.33, 3.15) O = 21, E = 9.93 PY = 7,959	O/E = 1.16 (95% CI = 0.55, 2.08) O = 9, E = 7.79 PY = 5,588	O/E = 0 (95% CI = 0, 2.7) O = 0, E = 1.38 PY = 1,647	O/E = 1.57 (95% CI = 1.07, 2.20) O = 30, E = 19.1 PY = 15,194
0.077–5.25 Mean = 0.449	O/E = 1.71 (95% CI = 1.00, 2.69) O = 16, E = 9.35 PY = 7,149	O/E = 2.87 (95% CI = 1.81, 4.29) O = 21, = 7.30 PY = 5,716	O/E = 2.86 (95% CI = 0.2, 12.6) O = 1, E = 0.35 PY = 544	O/E = 2.24 (95% CI = 1.60, 3.03) O = 38, E = 17.0 PY = 13,409

[a]Expected lung cancer deaths in this table are based on age-, race-, and calendar year-specific rates for the State of Maryland. The expected lung cancer deaths for those with race unknown was estimated from what would be expected if they had a race distribution similar to those for whom race was known. Cumulative exposure is lagged 5 years.

from 28.8 to 38.9 for trivalent chromium. Square root transformations gave a poorer fit than did log transformations of the cumulative exposure for both hexavalent and trivalent chromium using the same lag periods. Average exposure (cumulative exposure/duration of work) and log average exposure also gave poorer fits than did log transformations of the cumulative hexavalent and trivalent chromium exposure using the same lag periods. Log transformation of duration of work at the plant also resulted in a worse fit than did the untransformed variable for all lags. Based on the above results, log transformations of cumulative trivalent chromium exposure and cumulative hexavalent chromium exposure, and the untransformed duration of work, were utilized in all subsequent models.

Consideration of different lag times showed that for each of the three exposure measures, the 5- and 10-year lags gave essentially identical χ^2 values, with the 0- and 2-year lags slightly lower and the 20-year lag considerably lower (at least for the two chromium dose measures). A 5-year lag was selected for use in all models.

Cumulative hexavalent chromium exposure (mg/m^3-years), cumulative trivalent chromium exposure, and work years were found to be roughly equivalent in predictive ability when smoking (yes/no) was included in the model, and each of these exposure measures was significantly associated with increased lung cancer risk at the $P = 0.0001$ significance level (see Table VII). In Table VII, the coefficient of 0.325 (95% CI of 0.180–0.469) associated with $\log_{10}$ of cumulative hexavalent chromium exposure indicates that a 10-fold increase in cumulative exposure (or equivalently an increase of 1 in $\log_{10}$ cumulative exposure) increases the risk, or hazard, by a factor of exp (0.325) = 1.38 (95% CI of 1.20–1.63). This can be compared to an increase of exp (0.274) = 1.32 (95% CI of 1.15–1.51) fold following a 10-fold increase in cumulative trivalent chromium exposure. For work duration at the plant, the coefficient of 0.044 indicates that working 10 additional years increases the risk by a factor of exp (10 * 0.044) = 1.55.

The proportional hazards models were used to estimate risks by exposure quartile using the first quartile as the reference group. Using the median exposure in each quartile as the measure of cumulative hexavalent chromium exposure and with smoking included as a variable in the

TABLE VII. Results of Cox Models for Three Different Exposure Measures, Each Combined With Smoking Status; Chromium Chemical Production Workers, USA

Model	Variable	Coefficient (95% CI)	Relative risk	P-value	χ^2
I	Cigarette smoking	1.80 (0.80, 2.80)	6.05	0.0004	42.2
	Log_{10} cumulative hexavalent chromium exposure	0.325 (0.180, 0.469)	1.38[a]	0.0001	
II	Cigarette smoking	1.79 (0.79, 2.79)	5.99	0.0005	38.9
	Log_{10} cumulative trivalent chromium exposure	0.274 (0.140, 0.412)	1.32[a]	0.0001	
III	Cigarette smoking	1.75 (0.75, 2.75)	5.75	0.0006	36.4
	Years worked	0.044 (0.023, 0.065)	1.55[b]	0.0001	

[a] The relative risk is for each 10-fold increase in cumulative exposure.
[b] The relative risk is for each 10-year increase in years worked.

TABLE VIII. Cox Models for Cumulative Hexavalent Chromium Exposure/Cumulative Trivalent Chromium Exposure and Cumulative Hexavalent Chromium Exposure/Duration of Work (Smoking also Included in Each Model); Chromium Chemical Production Workers, USA

Model	Variable	Coefficient	Relative risk	P-value	χ^2
I	Log_{10} cumulative hexavalent chromium exposure	0.509	1.66[a]	0.045	42.8
	Log_{10} cumulative trivalent chromium exposure	−0.177	0.17[a]	0.449	
	Cigarette smoking	1.8	6.05	0.004	
II	Log_{10} cumulative hexavalent chromium exposure	0.256	1.29[a]	0.010	43.2
	Years worked	0.016	1.17[b]	0.303	
	Cigarette smoking	1.78	5.93	0.005	

[a] The relative risk is for each 10-fold increase in cumulative exposure.
[b] The relative risk is for each 10-year increase in years worked.

model, relative lung cancer risks of 1.83, 2.48, and 3.32 for persons in the 2nd, 3rd and 4th cumulative exposure quartiles, in comparison to the first quartile, were estimated.

There was a strong correlation between the log of cumulative hexavalent chromium and the log of cumulative trivalent chromium (Pearson correlation coefficient = 0.95; Spearman rank correlation coefficient = 0.95). There were also strong correlations between the log of cumulative hexavalent chromium exposure and work duration (Pearson correlation coefficient = 0.71; Spearman rank correlation coefficient = 0.87) and between the log of cumulative trivalent chromium exposure and work duration (Pearson correlation coefficient = 0.63; Spearman rank correlation coefficient = 0.84).

Despite these strong correlations, we attempted to separate the effects in two proportional hazards models (Table VIII). One model incorporated the log of cumulative hexavalent chromium exposure, the log of cumulative trivalent chromium exposure, and smoking. The other model incorporated the log of cumulative hexavalent chromium exposure, work duration, and smoking. In each case, inclusion of the other dose measure (log of cumulative trivalent chromium exposure or work duration) resulted in cumulative hexavalent chromium exposure still being statistically significant ($P < 0.05$) with the other measure not being statistically significant. In addition, the coefficient for work duration decreased substantially compared to the value in Table VII, and the coefficient for cumulative trivalent chromium exposure actually became negative.

A significant ($P < 0.05$) correlation of lung cancer with the occurrence of ulcerated nasal septum, perforated nasal septum, ulcerated skin, dermatitis, burn, and conjunctivitis was found using separate 2×2 tables. When smoking, cumulative exposure to hexavalent chromium, and the 10 potential clinical findings of chromium irritation were included in 10 separate proportional hazards models as covariates, none of the clinical findings of irritation were found to be significantly ($P < 0.05$) predictive of the occurrence of lung cancer, although perforated nasal septum and burn reached borderline significance ($P = 0.07$).

DISCUSSION

The current study confirms the elevated lung cancer risk from hexavalent chromium exposure observed in other studies and presents the best opportunity to date of evaluating the lung cancer exposure–response relationship from exposure to hexavalent chromium. A comparison of key attributes of the current study with those of the study by Mancuso [1975, 1997a] which has to date been the study most frequently used for exposure–response assessment of the lung cancer risk from hexavalent chromium is found in Table IX.

As can be seen, the current study, in comparison with the Mancuso study, had a larger cohort, more lung cancer deaths, and had smoking information for most of the cohort. Many of the exposure estimates of the current study are from direct measurements; a portion were from models using contemporary data. More important, however, the ambient measures or estimates of exposure were concurrent with the work history and are of hexavalent chromium directly, not derived from other measures. Furthermore, the cumulative exposure groups in the current study represent lower exposures than those of the Mancuso study, providing better risk estimates at these lower levels of exposure, an important consideration for quantitative risk assessment. Nonwhites were found to have higher mean cumulative hexavalent chromium exposures than whites (Table III). Nonwhites had somewhat longer mean work durations than did whites but not enough to account for the large difference between whites and nonwhites in mean cumulative exposure. The difference is more attributable to two different distributions of job titles biased toward jobs with higher exposures experienced by the nonwhite population.

The lung cancer risk among those with race unknown was less than expected (Table I). This may reflect the fact that cumulative hexavalent chromium exposure among those with race unknown was considerably less than among those whose race was known (Table III).

A high proportion of the cohort were smokers as were a high proportion of the lung cancer deaths. Only four of those who died from lung cancer did not smoke at the time of initial employment. Nevertheless, increasing exposure to hexavalent chromium was still a statistically significant risk factor when included with smoking as a covariate in the proportional hazards model. It was not possible to examine the interaction of smoking and cumulative hexavalent chromium exposure in the Cox regression because of the small number of nonsmoking lung cancer cases.

Considerable effort was made in the current study to develop estimates of trivalent chromium exposures from measured hexavalent chromium exposures and chemical analysis of settled dust and to use this information to evalvate whether there is a risk of lung cancer from cumulative trivalent chromium exposure. Analyses indicated that cumulative trivalent chromium exposure was not

TABLE IX. A Comparison of the Current Study with Studies by Mancuso [1975, 1997a]; Chromium Chemical Production Workers, USA

	Current study	**Mancuso [1975, 1997a]**
Cohort	1205 white males 848 nonwhite males 304 race unknown males	332 white males
Industrial hygiene measurements vis-a-vis work history	Concurrent with the work history	Not concurrent with work history (Measurements made in 1949 were used to estimate exposure to workers who began employment in 1931–37)
Industrial hygiene measurements vis-a-vis chromium species measurement	Cr^{+6} (Cr^3 derived from settled dust)	Total Cr (Cr^6 and Cr^3 derived from settled dust)
Number of lung cancer cases	122	42 (1975 study); 66 (1997 study)
Person-years of observation	70,736	5,853 (1975 study); 12,881 (1997 study)
Smoking data	Yes/No for 91% of cohort at time of first employment	None
Exposure groups (mg/m^3-years)	0–0.00149, 0.0015–0.0089, 0.009–0.0769, 0.077–5.25	< 0.25, 0.25–0.49, 0.50–1.00, 1.00–1.99, 2.00
Analysis of cancer risk of Cr VI and Cr III	Multivariate	Univariate